Health Canada Santé Canada

Your health and safety... our priority. *Votre santé et votre sécurité... notre priorité.*

Registration Decision RD2012-29

Ametoctradin

(publié aussi en français)

30 August 2012

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

ISSN: 1925-0932 (print)
1925-0940 (online)

Catalogue number: H113-25/2012-29E (print version)
H113-25/2012-29E-PDF (PDF version)

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2012

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

Registration Decision for Ametoctradin

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Initium Fungicide Technical, Zampro Fungicide and BAS 650 00 F Fungicide, containing the technical grade active ingredient ametoctradin, for use on brassica leafy vegetables, bulb vegetables, cucurbit vegetables, fruiting vegetables, leafy vegetables, hops, grapes and potatoes to control or suppress various diseases including downy mildew, late blight, and phytophthora.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2011-25, *Ametoctradin*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for ametoctradin and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2011-25. This decision is consistent with the proposed registration decision stated in PRD2011-25.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2011-25, *Ametoctradin* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

---

1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticide and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Ametoctradin?

Ametoctradin is a novel fungicidal compound present as the lone active ingredient in BAS 650 00 F Fungicide and as one of two components, along with dimethomorph, in the combination product Zampro Fungicide. Ametoctradin is a non-systemic and preventative compound used for foliar applications to manage plant diseases caused by water moulds. It acts on pathogen cells by interfering with their normal respiration process. BAS 650 00 F Fungicide and Zampro Fungicide are used on brassica leafy vegetables, bulb vegetables, cucurbit vegetables, fruiting vegetables, leafy vegetables, hops, grapes and potatoes to control or suppress various diseases including downy mildew, late blight, and phytophthora blight.

Health Considerations

Can Approved Uses of Ametoctradin Affect Human Health?

Products containing ametoctradin are unlikely to affect your health when used according to label directions.

Potential exposure to ametoctradin may occur through the diet (food and water), when handling and applying the product or when entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, the active ingredient ametoctradin was of low acute toxicity by the oral, dermal and inhalation routes. Ametoctradin was minimally irritating to the skin and the eyes and did not cause allergic skin reactions.

The end-use product, Zampro Fungicide, was of low acute toxicity via the dermal and inhalation routes. It was non-irritating to the eye and slightly irritating to the skin. Zampro Fungicide did not cause an allergic skin reaction. Zampro Fungicide was of moderate acute toxicity via the oral route; consequently the hazard signal words "WARNING-POISON" are required on the label.

The end-use product, BAS 650 00 F Fungicide, was of low acute toxicity by the oral, dermal and inhalation routes. It was non-irritating to the eye and slightly irritating to the skin and did not cause an allergic skin reaction.

The active ingredient ametoctradin did not cause cancer in animals and did not damage genetic material. There was no indication that ametoctradin caused damage to the nervous system or immune system. Ametoctradin did not cause birth defects in animals and there was no effect on the ability to reproduce. There was no indication of target organ toxicity. When ametoctradin was given to pregnant or nursing animals, no effects on the developing fetus or juvenile animal were observed.

The risk assessment ensures that the level of human exposure is well below the lowest dose at which no effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children one to two years old, the subpopulation which would ingest the most ametoctradin relative to body weight, are expected to be exposed to less than 1% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from ametoctradin is not of concern for all population sub-groups. Ametoctradin is not carcinogenic; therefore, a cancer dietary exposure assessment is not required.

Animal studies revealed no acute health effects. Consequently, a single dose of ametoctradin is not likely to cause acute health effects in the general population (including infants and children). An acute reference dose was not established, therefore, an acute dietary intake estimate is not required.

The Food and Drugs Act prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using ametoctradin on potatoes, dry bulb onions, green onions, head lettuce, leaf lettuce, spinach, celery, broccoli, cabbage, mustard greens, tomatoes, peppers, cucumber, cantaloupe, squash, grapes and hops were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of PRD2011-25.

Occupational Risks From Handling BAS 650 00 F Fungicide or Zampro Fungicide

Occupational risks are not of concern when BAS 650 00 F Fungicide or Zampro Fungicide are used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply BAS 650 00 F Fungicide or Zampro Fungicide, as well as field workers re-entering freshly treated fields, can come in direct contact with ametoctradin residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying BAS 650 00 F Fungicide or Zampro Fungicide must wear long pants, long-sleeved shirt and socks and shoes. During mixing, loading, clean-up and repair activities, workers must also wear chemical resistant gloves. For aerial application, the field crew and the mixer/loaders must wear chemical resistant gloves, coveralls and goggles or face shield during mixing/loading, clean-up and repair. The label also requires that workers do not enter treated fields for 12 hours after application for BAS 650 00 F Fungicide; restricted entry intervals for Zampro Fungicide (a co-formulation with dimethomorph) range from 12 hours to 20 days, depending on the crop and activity. The uses of the co-formulation are currently supported on the Canadian dimethomorph end-use product label. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, it was determined that the risks to these individuals are not a concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Ametoctradin Is Introduced Into the Environment?

When ametoctradin is applied as a preventative fungicide in field and vineyard crops, some of it finds its way into soil and water. Ametoctradin is only sparingly soluble in water and will quickly partition to sediments. However, ametoctradin is rapidly broken down by microbial activity in soil and water; thus, it is not expected to persist in the environment. Two of its four major transformation products (M650F03 and M650F04) will be present in soil and aquatic systems for a longer period of time. Laboratory studies indicate that ametoctradin is not mobile in soil, however its transformation products may be. In field studies conducted in Europe and North America, ametoctradin and its major transformation products M650F01, M650F02 and M650F03 were not detected at depth in the soil profile, indicating a minimal potential for groundwater contamination. However, the transformation product M650F04 was detected at depth and may therefore reach groundwater. In North American field studies, ametoctradin and three of the four major transformation products were not found in significant amounts at the beginning of the next growing season, however significant amounts of M650F04 can carry over. Although the transformation product M650F04 is persistent and may reach groundwater, it is unlikely to cause a risk to human health or the environment based on its toxicological profile. Ametoctradin is not volatile and is, therefore, not expected to be subject to long range transport in the atmosphere.

Ametoctradin can be applied by field sprayer, airblast sprayer or aerial application. There is a potential that non-target terrestrial and aquatic habitats may be exposed to the chemical as a result of spray drift or runoff. Ametoctradin presents a negligible risk to terrestrial organisms, including plants, beneficial insects (bees and other beneficial arthropods), birds and small mammals, at the use rates. Ametoctradin is not expected to pose a risk to aquatic invertebrates, amphibians or freshwater fish. Ametoctradin exposure can present a risk to freshwater algae and marine fish. In order to minimize the potential for exposure resulting from off-field drift, no-spray buffer zones will be required between the treated area and downwind aquatic habitats. No environmental risk was identified from exposure to ametoctradin's major transformation products.

Value Considerations

What Is the Value of BAS 650 00 F Fungicide and Zampro Fungicide?

BAS 650 00 F Fungicide and Zampro Fungicide are preventative fungicides effective in the control or suppression of many important plant diseases caused by water moulds.

BAS 650 00 F Fungicide and Zampro Fungicide provide effective solutions to manage commercially important diseases such as downy mildew on brassica leafy vegetables, bulb vegetables, cucurbit vegetables, leafy vegetables, grapes, and hops, late blight on potatoes and fruiting vegetables, and phytophthora blight on cucurbit vegetables and fruiting vegetables. Ametoctradin provides users with a new fungicidal mode of action with no documented cross-resistance with other fungicidal active ingredients used in controlling water mould diseases. In addition, because ametoctradin is combined with dimethomorph in Zampro Fungicide, a single application of this product provides a dual mode of action, thereby reducing the probability of disease resistance development. Moreover, some of the diseases shown to be sensitive to BAS 650 00 F Fungicide and Zampro Fungicide, such as phytophthora blight, have very limited options for their control in terms of currently registered products.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of BAS 650 00 F Fungicide and Zampro Fungicide to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

As there is a concern with users coming into direct contact with ametoctradin on the skin or through inhalation of spray mists, anyone mixing, loading and applying BAS 650 00 F Fungicide or Zampro Fungicide must wear long pants, a long-sleeved shirt and socks and shoes. During mixing, loading, clean-up and repair activities, workers must also wear chemical-resistant gloves. For aerial application, the field crew and the mixer/loaders must wear chemical-resistant gloves, coveralls and goggles or face shield during mixing/loading, clean-up and repair. In addition, standard label statements to protect against drift during application are required.

Environment

To protect sensitive aquatic species from the use of ametoctradin, mitigation measures are required on the label. These include adding precautionary statements to the label regarding environmental hazards and the directions for use, as well as no-spray buffer zones of up to 10 m for freshwater habitats and 1 m for marine habitats to mitigate potential exposures via spray drift.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2011-25, *Ametoctradin*) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.